IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Christoph H. Benning *et al.*
Serial No.: 09/709,020 Group No.: 1645
Filed: 11/08/2000 Examiner: Y. Pak
Entitled: **Compositions And Methods For The Synthesis And Subsequent Modification Of Uridine-5'-Diphosphosulfoquinovose (UDP-SQ)**

#6
B.G.J
10/16/01

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Dated: October 5, 2001 By: Traci E. Light

Sir or Madam:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following printed publications are referred to in the body of the specification:

- U.S. Patent No. 6,091,003 to Nagai C & Nan G;[1]
- U.S. Patent No. 5,584,807 to McCabe;
- U.S. Patent No. 5,374,716 to Biermann *et al.*;
- U.S. Patent No. 4,965,188 to Mullis *et al.*;
- U.S. Patent No. 4,683,202 to Mullis;

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[1] A hard copy of this reference has not been included because a search of the U.S. PTO database indicated that said numbered patent had been withdrawn. No further information was available.

- U.S. Patent No. 4,683,195 to Mullis *et al.*;
- Anderson and Young, Quantitative Filter Hybridization, *in Nucleic Acid Hybridization* (1985);[2]
- Ausubel, *et al.*, ed., *Short Protocols in Molecular Biology*, John Wiley & Sons, NY (1992);[3]
- Becker, D., "Binary vectors which allow the exchange of plant selectable markers and reporter genes," *Nucleic Acids Res.* 18:203 (1990);
- Benson, A.A., "The Plant Sulfolipid," *Adv. Lipid Res.* 1:387-394 (1963);
- Black *et al.*, "Analysis of a Het- mutation in Anabaena sp. PCC7120 implicates a secondary metabolite in the regulation of heterocyst spacing," *J. Bacteriol.*, 174:2282-2292 (1994);
- Clough, S. and Bent, A., "Floral dip: a simplified method for Agrobacterium-mediated transformation of *Arabidopsis thaliana*," *Plant J.*, 16: 735-43 (1998);
- Dieffenbach and Dveksler, *PCR Primer, a Laboratory Manual*, Cold Spring Harbor Press, Plainview, NY (1995);[4]
- Essigman *et al.*, "Phosphate Availability Affects the Thylakoid Lipid Composition and Expression of SQD1, a Gene Required for Sulfolipid Biosynthesis in *Arabidopsis thaliana*," *Proc. Natl. Acad. Sci. USA*, 95:1950-955 (1998);
- Gordon-Kamm *et al.*, "Transformation of Maize Cells and Regeneration of Fertile Transgenic Plants," *Plant Cell*, 2:603-618 (1990);
- Gustafson *et al.*, "AIDS-Antiviral Sulfolipids From Cyanobacteria (Blue-Green Algae)," *J. Natl. Cancer Inst.*, 81:1254-1258 (1989);

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[2] Because this is a general text that was cited in the specification without direction to any specific page, applicants have not included any excerpts with this IDS.

[3] Because this is a general text that was cited in the specification without direction to any specific page, applicants have not included any excerpts with this IDS.

[4] Because this is a general text that was cited in the specification without direction to any specific page, applicants have not included any excerpts with this IDS.

- Heinz *et al.*, "Synthesis of different nucleoside 5'-diphospho-sulfoquinovoses and their use for studies on sulfolipid biosynthesis in chloroplasts," *Eur. J. Biochem.*, 184:445-453 (1989);
- Howard and Bethell, *e.g.*, *Basic Methods in Antibody Production and Characterization*, CRC Press, (2000);[5]
- Logemann *et al.*, "Improved Method for the Isolation of RNA from Plant Tissues," *Anal. Biochem.*, 163:16-20 (1987);
- Miyano, M. & Benson, A.A., "The Plant Sulfolipid VII. Synthesis of 6-sulfo-α-D-quinovopyranosyl-(1→1')-glycerol and Radiochemical Synthesis of Sulfolipids," *J. Am. Chem. Soc.*, 84:59-62 (1962);
- Ohta *et al.*, "Sulfoquinovosyldiacylglycerol, KM043, a new potent inhibitor of eukaryotic DNA polymerases and HIV-reverse transcriptase type 1 from a marine red alga, *Gigartina tenella*," *Chem. Pharm. Bull.*, 46(4):684-86 (1998) [abstrct only];
- Ohta *et al.*, "Action of a New Mammalian DNA Polymerase Inhibitor, Sulfoquinovosyl diacylglycerol," *Biol. Pharm. Bull.*, 22(2):111-16 (1999);
- Prentki, P. and Krisch, H.M., "In vitro insertional mutagenesis with a selectable DNA fragment," *Gene*, 29:303-313 (1984);
- Roy, A.B. & Hewlins, J.E., "Sulfoquinovose and its aldonic acid: their preparation and oxidation to 2-sulfoacetaldehyde by periodate," *Carbohydrate Res.*, 302:113-117 (1997);
- Sambrook, *et al.*, *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, New York, pp. 16.7-16.8 (1989);
- Shirahashi *et al.*, "Isolation and Identification of Anti-tumor-Promoting Principles from the Fresh-Water Cyanobacterium *Phormidium tenue*," *Chem. Pharm. Bull.*, 41(9):1664-66 (1993); and
- von Schaeven, A., Ph.D. thesis, Freie Universität Berlin (1989)[6]

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[5] Because this is a general text that was cited in the specification without direction to any specific page, applicants have not included any excerpts with this IDS.

[6] The applicant has been unable to obtain a copy of this thesis, but if the examiner so request we will try to obtain it.

- Wolk *et al.*, "Construction of shuttle vectors capable of conjugative transfer from *Escherichia coli* to nitrogen-fixing filamentous cyanobacteria," *Proc. Natl. Acad. Sci. USA*, 81:1561-565 (1984).

Applicants have become aware of the following printed publications which may be material to the examination of this application:

- Bechtold *et al.*, "*In planta Agrobacterium* mediated gene transfer by infiltration of adult *Arabidopsis thaliana* plants," *C.R. Acad. Sci. Paris*, 316:1194-1199 (1993), discloses a method for the *in situ* transformation of *Arabidopsis thaliana* using *Agrobacterium*. The reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphospho sulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.
- Benning C, "Biosynthesis and Function of the Sulfolipid Sulfoquinovosyl Diacylglycerol, "*Annu. Rev. Plant Physiol. Plant Mol. Biol.*, 49:53-75 (1998), discloses a hypothesis for the synthesis and function of the sulfolipid sulfoquinovosyl diacylglycerol. However, the reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.
- Benning *et al.*, "Accumulation of a Novel Glycolipid and a Betaine Lipid in Cells of *Rhodobacter sphaeroides* Grown under Phosphate Limitation," *Arch. Biochem. & Biophys.*, 317:103-111 (1995), discloses the structure of two lipids, glucosylgalactosyl diacylglycerol and digalactosyl *N*-trimethyl homoserine, which are only synthesized under phosphate-limiting conditions in the cells of

R. sphaeroides. However, the reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphospho sulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.

- Benning *et al.*, "The sulfolipid sulfoquinovosyldiacylglycerol is not required for photosynthetic electron transport in *Rhodobacter sphaeroides* but enhances growth under phosphate limitation," *Proc. Natl. Acad. Sci. (USA)*, 90:1561-65 (1993), discloses the insertional inactivation of the *sqdB* gene in *R. sphaeroides* resulting in a null mutant unable to synthesize sulfolipids (*i.e.* a sulfolipid-deficient mutant). However, the reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.
- Browse *et al.*, "Fluxes through the prokaryotic and eukaryotic pathways of lipid synthesis in the '16:3' plant *Arabidopsis thaliana*," *J. Biochem.*, 235:25-31 (1986), discloses the use of the positional analyses of individual lipids to measure the fluxes through the prokaryotic and eukaryotic pathways during lipid synthesis in *A. thaliana*. However, the reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.
- Benning C & Somerville CR, "Isolation and Genetic Complementation of a Sulfolipid-Deficient Mutant of *Rhodobacter sphaeroides*," *J. Bacteriol.*,

174(7):2352-2360 (1992), discloses the screening of *R. sphaeroides* mutants deficient in sulfolipid accumulation for altered sulfolipid content, and the isolation of a gene involved in sulfolipid biosynthesis (*i.e. sqdA*) by complementation. However, the reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated. The reference also does not disclose the oligonucleotide sequences of said first and second peptides.

- Chen L & Li H, "A mutant deficient in the plastid lipid DGD is defective in protein import into chloroplasts," *The Plant J.*, 16(1):33-39 (1998), discloses that chloroplasts isolated from an *Arabidopsis thaliana* mutant deficient in the plasid lipid digalactosyl diacylglycerol (DGD) were normal in importing a chloroplast outer membrane protein, but were defective in importing precursor proteins targeted to the interior of the chloroplasts. However, the reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.
- Dörmann *et al.*, "*Arabidopsis* Galactolipid Biosynthesis and Lipid Trafficking Mediated by DGD1," *Science*, 284:2181-2184 (1999), discloses the reconstitution of the galactolipid biosynthetic pathway in *E. coli* utilizing the gene product of the *Arabidopsis* DGD1 (digalactosyldiacylglycerol 1) gene. The reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second

peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.

- Dörmann *et al.*, "Isolation and Characterization of an Arabidopsis Mutant Deficient in the Thylakoid Lipid Digalactosyl Diacylglycerol," *The Plant Cell*, 7:1801-10 (1995), discloses that the transfer of galactose from UDP-galactose to diacylglycerol, to form monogalactosyl diacylglycerol (MGD), is catalyzed by the UDP-galactose:diacylglycerol galactosyltransferase. The reference also discloses that the assembly of digalactosyl diacylglycerol (DGD) is catalyzed by the galactolipid:galactolipid galactosyltransferase. However, the reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.
- Güler *et al.*, "A Null Mutant of *Synechococcus* sp. PCC7942 Deficient in the Sulfolipid Sulfoquinovosyl Diacylglycerol," *J. Biol. Chem.*, 271(13):7501-7507 (1996), discloses the isolation and characterization of the putative *sqdB*-like gene of *Synechococcus* sp. PCC7942. The reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.
- Hanashima *et al.*, "Structural determination of sulfoquinovosyldiacylglycerol by chiral syntheses," *Tetrahedron Letters*, 41:4403-4407 (2000), discloses a chiral synthetic method used to obtain the (2*R*) and (2*S*) analogues of sulfoquinovosyldiacylglycerol in order to determine the C-2 stereochemistry of the naturally-occurring compound. The reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphospho

sulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.

- Newman *et al.*, "Genes Galore: A Summary of Methods for Accessing Results from Large-Scale Partial Sequencing of Anonymous *Arabidopsis* cDNA Clones," *Plant Physiol.*, 106:1241-1255 (1994), discloses the generation numerous *Arabidopsis* cDNA clones from plant cells and tissues, and DNA sequence analysis (*e.g.* BLAST alignment) of said clones including the identification of various expressed sequence tags (ESTs). The reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated. The reference also does not disclose the oligonucleotide sequences of said first and second peptides.
- Ohta *et al.*, "Studies on a novel DNA polymerase inhibitor group, synthetic sulfoquinovosylacylglycerols: inhibitory action on cell proliferation," *Mutation Rsch.*, 467:139-152 (2000), discloses the effects of sulfoquinovosyl mono- and di-acylglycerols on DNA polymerases α and β in mammalian cells. The reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.
- Rossak *et al.*, "Accumulation of UDP-sulfoquinovose in a Sulfolipid-deficient Mutant of *Rhodobacter sphaeroides*," *J. Biol. Chem.*, 270(43):25792-25797 (1995), discloses that the inactivation of the *R. sphaeroides* sqdD gene results

in a sulfolipid-deficient mutant, and suggests that said gene acts as a UDP-sulfoquinovose:diacylglycerol sulfoquinovosyltransferase. The reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated. The reference also does not disclose the oligonucleotide sequences of said first and second peptides.

- Roy AB & Hewlins MJE, "An improved preparation of cyclohexylammonium allyl and D-glycer-1'-yl 6-deoxy-6-*C*-sulfonato-α-D-glucopyranosides," *Carbohydrate Rsch.*, 310:173-176 (1998), discloses a procedure for the oxidation of allyl α-sulfoquinovoside to DL-glycer-1'-yl 6-deoxy-6-*C*-sulfo-α-D-glucopyranoside by potassium permanganate followed by the crystillization of cyclohexylammonium D-glyceryl α-sulfoquinovoside. The reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.
- Sanda *et al.*, "Enzymatic Action of SQD1 - A protein involved in Sulfolipid Headgroup Biosynthesis," Abstract & Poster, presented at the annual meeting for the *American Society for Plant Physiologists*, July 15, 2000, suggests that the enzyme SQD1 catalyzes the *in vitro* synthesis of UDP-sulfoquinovose (UDP-SQ) from UDP-glucose (UDP-G) and an appropriate sulfur donor, and that UDP-SQ is involved in the biosynthesis of SQDG. The reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a

nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated. The reference also does not disclose the oligonucleotide sequences of said first and second peptides.

- Sinan Güler, "Genetische Analyse der Funktion des Sulfolipids Sulfoquinovosyl diacylglycerin in Organismen mit oxygener Photosynthese," Dissertation (1996), discloses that the bacterial (*R. sphaeroides*) *sqdB* and the plant (*A. thaliana*) *SQD1* genes encode highly conserved proteins involved in the biosynthesis of the UDP-sulfoquinovose headgroup donor for sulfolipid biosynthesis. The reference also discloses the isolation and characterization of the putative *sqdB*-like gene of *Synechococcus* sp. PCC7942. The reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.
- Bernd Essigmann, "Sulfolipid in Arabidopsis thaliana: Biosynthese, Regulation und Funktion," Dissertation (1999), discloses the expression of recombinant SQD1 protein in *E. coli*, and a three-dimensional atomic model of the SQD1 gene of *A. thaliana* using the crystallographic structure of UDP-glucose 4-epimerase as a template, along with a predicted NAD^+ binding site. The reference does not disclose a method wherein uridine-5'-diphosphoglucose is converted to uridine-5'-diphosphosulfoquinovose using sulfite and a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6, followed by the transfer of said sulfoquinovose to diacylglycerol using a second peptide encoded by a nucleic acid set forth in SEQ ID NO:1 such that sulfoquinovosyl diacylglycerol is generated.

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: October 5, 2001

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